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EXAMINER

NOGUEROLA, ALEXANDER STEPHAN

ART UNIT PAPER NUMBER

1753

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/075,404

Applicant(s)

JOHNSON ET AL.

Examiner

ALEX NOGUEROLA

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-40 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 23-40 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 02/17/2005.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: ____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed August 02, 2005 have been fully considered but they are not persuasive.

The rejections of claims 23 and 24 as being obvious under 35 U.S.C. 103(a) over Liu in view of Knox and McCormick

Applicants assert, "Liu lacks **any** motivation, whatsoever, to make the combination of the cited documents." Liu is the base reference for the rejections. The examiner is not aware of any requirement under 35 U.S.C. 103(a) that the base reference must provide motivation for using the teachings of a secondary reference. Applicants also assert, 'At page 1668, first full paragraph, Liu refers to another publication that specifically notes "the other fragments of 23 kbp were **successfully separated** using this ultra-diluted HEC solution under **constant filed strength**.' The examiner has not found the quoted clause. In any event as acknowledged by Applicants this quotation is from another publication. So its relvence to limiting how Liu performs capillary electrophoresis is not apparent.

Applicants also assert, 'Clearly, there is no motivation whatsoever to combine Liu with the other cited art, even if, as the Examiner alleges, "as a general principle it was known in the art at the time of the invention that a high ramp rate would adversely affect the separation resolution of a capillary electrophoresis system.'" The stated general principle is the motivation. Liu's injection voltage is 3000 V for 4 s and the run voltage is 6,000 volts. See Figure 2 caption. This run voltage is achieved either very quickly, that is the voltage has a very high ramp rate from 3000V, or at a slow ramp rate. Liu does not mention a slow controlled voltage ramp rate. Therefore, the fairest assumption is that Liu achieves the 6,000 volts very quickly, that is, at a very high ramp rate.¹ As discussed in detail by Knox this will adversely affect the separation results. McCormick was cited just to show it was known at the time of the invention how to evaluate the effect of different ramp rates on separation resolution. It is noteworthy that McCormick uses a voltage ramp to reduce peak broadening as recited in the preambles of claims 23 and 25, albeit not for nucleic acids.

¹ It should be noted that Bio-Focus 3000 electrophoresis system, which was used by Liu (see Experimental Section – Instrumentation and Materials on page 1669), is configured for optional voltage ramping (see page 5-3 and pages 5-59 to 5-65 of the Operating Manual).

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Applicants also assert, 'merely, because one of skill in the art might know, as the Examiner alleges, how to "evaluate" the effect of different ramp rates on separation resolution, nothing in Knox points to actually using the ramp rate as claimed in the method of claims 24 or 25.' The examiner respectfully disagrees, once changing the ramp rate has been identified as being beneficial to the electrophoresis separation and how to evaluate the effect different ramp rates has been taught then selecting a particular ramp rate, barring a contrary showing, such as unexpected results, is just optimization: "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).' MPEP 2144.05II.A. Applicants comment is curious in light of the fact that they have added two new claims with a range of ramp rates (claims 29 and 37).

Thus, the rejections of claims 23 and 24 under 35 U.S.C. 103(a) are maintained.

Applicants have correctly pointed out that "Virtanen" on page 7 of the Office action of February 03, 2005 should be -- McCormick --.

Status of the Rejections Pending since the Office action of February 03, 2005

2. The double patenting rejection of claim 22 is withdrawn, as the claim has been cancelled.

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3. The double patenting rejection of claim 23 is maintained.
4. The rejection of claim 22 under 35 U.S.C. 102(b) is withdrawn, as the claim has been cancelled.
5. The rejection of claims 23 and 24 under 35 U.S.C. 103(a) are maintained.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claim 23 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,372,106 B1 in view of Knox et al. ("Volume Expansion and Loss of Sample due to Initial Self-heating in Capillary Electroseparation (CES) Systems," *Chromatographia* vol. 38, no. 5/6, March 1994) ("Knox") and McCormick ("Capillary Zone Electrophoretic Separation of Peptides and Proteins Using Low pH Buffers in Modified Silica Capillaries," *Anal. Chem.* 1988,

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60, 2322-2328) ("McCormick "). Claim 1 of U.S. Patent No. 6,372,106 B1 meets all of the limitations of claim 23 of the instant application except that it does not specify a ramp rate, particularly the ramp rate of claim 23². McCormick discloses a capillary electrophoresis method using a ramp rate of 0.70 V/(cm-s) (capillary length = 110 cm, run voltage = 23kV (from injection voltage of 2kV), and rise time = 300s). See the abstract; Electrophoresis on page 2322; Figure 1; Figure 12; and the second full paragraph in the first column on page 2327. It would have been obvious to one with ordinary skill in the art at the time the invention was made to use a slow ramp rate, particularly within the claimed rate interval, as taught by McCormick in the invention of claim 1 because as taught by McCormick resolution will be improved with a decreased ramp rate. See the paragraph at the bottom of the second column on page 62 and continue onto page 63. This is also consistent with Knox who broadly demonstrates how a rapid ramp rate can adversely affect the separation resolution in a capillary electroseparation system. See the abstract.

² The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). Thus « separation medium » as used in claim 1 of US 6,372,106 B1 includes a non-crosslinked medium. See column 3, line 65 – column 4, line 2 in US 6,372,106 B1.

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8. Claims 25-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,372,106 B1 in view of Knox et al. ("Volume Expansion and Loss of Sample due to Initial Self-heating in Capillary Electroseparation (CES) Systems," *Chromatographia* vol. 38, no. 5/6, March 1994) ("Knox") and McCormick ("Capillary Zone Electrophoretic Separation of Peptides and Proteins Using Low pH Buffers in Modified Silica Capillaries," *Anal. Chem.* 1988, 60, 2322-2328) ("McCormick "). Claim 23, from which claims 25-32 ultimately depend, has been addressed above. Barring a contrary showing, all of these claims only provide for optimized ranges or values. The length of time the electrophoresis is performed (run time) just depends on how long it takes for all the sample of interest to be separated and detected. The ramp rate, as discussed in the rejection of claim 23, is just a matter of optimizing the electrophoresis run for peak broadening. Reduced peak broadening will of course improve resolution of the sample components. So the amount that peak broadening is reduced will just depend on the desired measurement accuracy of the sample components.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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12. The rejection of claims 23 and 24 is restated below for Applicants convenience.

One change has been made though, "Viratanen" has been replaced with

-- McCormick --.

13. Claims 23, 24, 27-32, and 35-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. ("Separation of Double- and Single-stranded DNA Restriction Fragments: Capillary Electrophoresis with Polymer Solutions under Alkaline Conditions," *Anal. Chem.* 1999, 71, 1668-1673) ("Liu") in view of Knox et al. ("Volume Expansion and Loss of Sample due to Initial Self-heating in Capillary Electro separation (CES) Systems," *Chromatographia* vol. 38, no. 5/6, March 1994) ("Knox") and McCormick ("Capillary Zone Electrophoretic Separation of Peptides and Proteins Using Low pH Buffers in Modified Silica Capillaries," *Anal. Chem.* 1988, 60, 2322-2328) ("McCormick").

Addressing claims 23 and 24, Liu discloses an electrophoresis method in which nucleic acid is separated by differential migration through a buffered solution containing a non-crosslinked polymer under the influence of a run field. See the abstract; Experimental Section on page 1669; and Figure 2. Liu does not mention the ramp rate used; however, as a general principle it was known in the art at the time of the invention that a high ramp rate would adversely affect the separation resolution of a capillary electrophoresis system. See the Knox article, which explains in detail why the ramp rate is important to separation resolution. It was also known at the time of the invention how to evaluate the effect of different ramp rates on separation resolution. See in

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McCormick the abstract; Electrophoresis on page 2322; Figure 1; Figure 12; and the second full paragraph in the first column on page 2327. It was further known to use a ramp rate of no greater than $5\text{V}/(\text{cm}\cdot\text{s})$. See the passages already cited in McCormick and note that McCormick discloses a capillary electrophoresis method using a ramp rate of $0.70\text{ V}/(\text{cm}\cdot\text{s})$ (capillary length = 110 cm, run voltage = 23kV (from injection voltage of 2kV), and rise time = 300s). Although McCormick does not mention using a non-crosslinked polymer or nucleic acid it should be noted that McCormick does disclose coating the inside of the capillary with polymer and separating proteins. See the abstract and Capillary Modification on page 2322. Thus, in light of the teaching of Knox and McCormick barring a contrary showing, such as unexpected results, Applicants ramp rate of "no greater than $5\text{ V}/\text{cm}\cdot\text{s}$ " is just an optimized ramp rate.

Addressing claims 27-32 and 35-40, barring a contrary showing, all of these claims only provide for optimized ranges or values. The length of time the electrophoresis is performed (run time) just depends on how long it takes for all the sample of interest to be separated and detected. The ramp rate, as discussed in the rejection of claims 23 and 24, is just a matter of optimizing the electrophoresis run for peak broadening. Reduced peak broadening will of course improve resolution of the sample components. So the amount that peak broadening is reduced will just depend on the desired measurement accuracy of the sample components.

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14. Claims 25, 26, 33, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. ("Separation of Double- and Single-stranded DNA Restriction Fragments: Capillary Electrophoresis with Polymer Solutions under Alkaline Conditions," *Anal. Chem.* 1999, 71, 1668-1673) ("Liu") in view of Knox et al. ("Volume Expansion and Loss of Sample due to Initial Self-heating in Capillary Electro separation (CES) Systems," *Chromatographia* vol. 38, no. 5/6, March 1994) ("Knox") and McCormick ("Capillary Zone Electrophoretic Separation of Peptides and Proteins Using Low pH Buffers in Modified Silica Capillaries," *Anal. Chem.* 1988, 60, 2322-2328) ("McCormick") as applied to claims 23 and 24 above, and further in view of the CAPLUS abstract of Isaaq et al. ("The effect of column length, applied voltage, gel type, and concentration on the capillary electrophoresis separation of DNA fragments and polymerase chain reaction products," *Electrophoresis* (1997), 18(7), 1153-1158) ("Isaaq"). Claims 25, 26, 33, 34 provide for different run field ranges. Liu uses a run field of 6kV, which is outside the claimed ranges. Although, it should be noted that the Operating Manual for the Bio-Focus 3000 capillary electrophoresis system, which was used by Liu, states, "To achieve both good separation and resolution in a short time, voltage field strengths of over a thousand volts per centimeter 930,000 volts total) can be applied, although many routine separations are usually performed at 150-400 V/cm field strength." See page 1-5. As shown by Isaaq it that applied voltage will affect the migration time and resolution of nucleic acids. Thus, barring a contrary showing, a run voltage within one of the claimed ranges is just optimizing the electrophoresis separation. "[W]here the general conditions of a claim are disclosed in the prior art, it is

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not inventive to discover the optimum or workable ranges by routine experimentation.”

In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).’ MPEP 2144.05II.A.

European Search Report for Application No. EP 04013127 ('Search Report')

15. US 5,385,654 A was cited as an “X” reference against claims 1-10 in the Search Report. Independent claims 23 and 24 require “establishing the run field at a ramp rate no greater than about 5 V/cm-s.” US 5,385,654 A discloses ramping the *temperature*, but not the run voltage. Electrokinetic injection and electrophoresis are performed under constant voltage. See col. 3:21-40 and col. 8:22-25.

16. US 5,409,586 A was cited as an “X” reference against claims 1-10 in the Search Report. Independent claims 23 and 24 require “establishing the run field at a ramp rate no greater than about 5 V/cm-s.” US 5,409,586 A discloses programming the *temperature*, but not the run voltage. Electrokinetic injection and electrophoresis are performed under constant voltage. See col. Col. 12:Table 2; col. 12:66 – col. 13:17; col. 14: Table 3; and col. 16:Table 4.

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17. Although only cited as an "A" reference it should be noted that US 5,221,448 A does disclose ramping the run field. However this is done to control temperature for performing thermal gradient electrophoresis, not to reduce peak broadening as the run field is established. Also, the ramp rate is substantially higher than 5V/cm-s as claimed. US 5,221,448 A discloses a capillary length of 10-200 cm long and an initial ramp rate of 3KV/sec. See the abstract; col. 1:7-12; col. 6:43-50; and col. 11:59 – col. 12:35. For a capillary length of 200 cm the initial ramp rate is 15 V/cm-sec. A second ramping rate is applied at twice the first ramp rate. See col. 12:21-23.

Final Rejection

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Alex Nogueraola
Primary Examiner
AU 1753
October 6, 2005